REMARKS

The specification has been amended to provide a unique sequence identification number for each nucleotide sequence within the specification. The attached sequence listing has also been inserted into the application. No new matter is introduced by any of the amendments.

CONCLUSION

Applicants submit that this application is now in condition for allowance, and such action is respectfully requested. A marked-up version indicating the amendments made to the specification, as required by 37 C.F.R. § 1.121(b)(1)(iii), is enclosed.

If there are any charges, or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

Date: 16 August 2001

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Guy Beardsley
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Rima Rozen	Art Unit:	Not Yet Assigned
Serial No.:	Not Yet Assigned	Examiner:	Not Yet Assigned
Filed:	August 16, 2001	Customer No.:	21559
Title:	cDNA FOR HUMAN METHYLENETETRAHYDROFOLATE REDUCTASE AND USES THEREOF		

Assistant Commissioner For Patents
Washington, D.C. 20231

Version with Markings to Show Changes Made

A marked-up version of the first paragraph of the specification is presented below.

"This application is a divisional of pending US patent application serial number 09/592,595 filed June 12, 2000, which is a continuation-in-part of US patent application serial number 09/258,928 filed March 1, 1999 (now US patent number 6,218,120), which is a continuation in part of US patent application serial number 08/738,000 filed February 12, 1997 (now US patent number 6,074,821), which claims priority from PCT CA 95/00314, filed May 25, 1995, and GB 9410620.0, filed May 26, 1994."

A marked-up version of the paragraph on page 60, line 8, through page 61, line 9, of the specification is presented below.

"Patients with spina bifida and mothers of patients were recruited from the Spina Bifida Clinic at the Montreal Children's Hospital following approval from the Institutional Review Board. Control children and mothers of controls were recruited from the same institution. Blood samples were used to prepare DNA from peripheral leukocytes, to assay MTHFR activity in lymphocyte extracts, and to measure total plasma homocysteine (tHcy). The presence of the C677T mutation (A to V) was evaluated by PCR and HinfI digestion (2). The A1298C mutation was initially examined by PCR and MboII digestion (5). The silent mutation, T1317C, was identified by SSCP and sequence analysis in a patient with severe MTHFR deficiency and homocystinuria. This patient, an African-American female, already carries a previously-described splice mutation (patient 354 (8)). Since this mutation also creates a MboII site and results in a digestion pattern identical to that of the A1298C mutation, distinct artificially-created restriction sites were used to distinguish between these 2 mutations. Detection of the A1298C polymorphism was performed with the use of the sense primer 5'-GGGAGGAGCTGACCAGTGCAG-3' (SEQ ID NO:15) and the antisense primer (5'-GGGGTCAGGCCAGGGGCAG-3', SEQ ID NO:16), such that the 138bp PCR fragment was digested into 119bp and 19bp fragments by Fnu4HI in the presence of the C allele. An antisense primer (5'-GGTTCTCCCGAGAGGTAAAGATC-3', SEQ ID NO:17), which introduces a TaqI site, was similarly designed to identify the C allele of the T1317C polymorphism. Together with a sense primer (5'-CTGGGGATGTGGTGGCACTGC-3', SEQ ID NO:18), the 227bp fragment is digested into 202bp and 25bp fragments."